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<110> ProChon Biotech Ltd.  
Yayon, Avner

<120> TREATMENT OF T CELL MEDIATED DISEASES BY INHIBITION OF FGFR3

<130> PRO-028-PCT

<140> PCT/IL04/00528

<141> 2004-06-17

<150> IL156495

<151> 2003-06-17

<150> US60/490,961

<151> 2003-07-30

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<170> PatentIn version 3.2

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Gln Ser Tyr Asp Gly Pro Asp Leu Trp  
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Gln Ser Tyr Asp Tyr Ser Ala Asp Tyr  
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Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Gly Arg Gly Leu Glu  
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Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala  
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Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn  
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val  
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Tyr Tyr Cys Ala Arg Ser Tyr Tyr Pro Asp Phe Asp Tyr Trp Gly Gln  
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Gly Thr Leu Val Thr Val Ser Ser  
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35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr  
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Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
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Leu Val Thr Val Ser Ser  
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Gly Val Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu  
35 40 45

Trp Leu Ala Leu Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser  
50 55 60

Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val  
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr  
85 90 95

Cys Ala Arg Tyr His Ser Trp Tyr Glu Met Gly Tyr Tyr Gly Ser Thr  
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Val Gly Tyr Met Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val  
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Ser Ser  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe  
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Gln Gly Arg Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr Met  
65 70 75 80

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala  
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Arg Asp Asn Trp Phe Lys Pro Phe Ser Asp Val Trp Gly Gln Gly Thr  
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Leu Val Thr Val Ser Ser  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
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Ala Arg Val Asn His Trp Thr Tyr Thr Phe Asp Tyr Trp Gly Gln Gly  
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Thr Leu Val Thr Val Ser Ser  
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr  
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Gly Tyr Trp Tyr Ala Tyr Phe Thr Tyr Ile Asn Tyr Gly Tyr  
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Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr  
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Thr Trp Gln Tyr Ser Tyr Phe Tyr Tyr Leu Asp Gly Gly Tyr  
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Tyr Phe Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr  
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Asn Met Ala Tyr Thr Asn Tyr Gln Tyr Val Asn Met Pro His  
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Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr  
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Ser Met Asn Ser Thr Met Tyr Trp Tyr Leu Arg Arg Val Leu  
100 105 110

Phe Asp His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
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Asp Ile Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln  
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Thr Ala Arg Ile Ser Cys Ser Gly Asp Ala Leu Gly Asp Lys Tyr Ala  
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu  
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Gly Pro Asp Leu Trp  
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Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln  
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Asp Ile Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln  
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Thr Ala Arg Ile Ser Cys Ser Gly Asp Ala Leu Gly Asp Lys Tyr Ala  
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu  
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Tyr Ser Ala Asp Tyr  
85 90 95

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln  
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Thr Ala Arg Ile Ser Cys Ser Gly Asp Ala Leu Gly Asp Lys Tyr Ala  
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu  
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Phe Asp Phe Ala Val  
85 90 95

Phe Gly Gly Thr Lys Leu Thr Val Leu Gly Gln  
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Glu Arg Ala Thr Ile Asn Cys Arg Ser Ser Gln Ser Val Leu Tyr Ser  
20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln  
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val  
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln  
85 90 95

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Lys Arg Thr  
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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser  
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu  
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Ala Arg Phe Ser  
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu  
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Ser Asn Tyr Pro  
85 90 95



Asp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr  
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Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr  
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu  
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe  
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu  
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Asn Asn  
85 90 95

Ser Asp Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln  
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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser  
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Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu  
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Ala Arg Phe Ser  
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu  
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Asn Asn Ala Pro  
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Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr  
100 105 110

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Thr Ala Arg Ile Ser Cys Ser Gly Asp Ala Leu Gly Asp Lys Tyr Ala  
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu  
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Tyr Phe Lys Leu Val  
85 90 95

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln  
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35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe  
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu  
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Met Tyr  
85 90 95

Asn Tyr Ile Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln  
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Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser  
35 40 45

Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn Gln Phe  
50 55 60

Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val Tyr Tyr  
65 70 75 80

Cys Ala Arg Ser Tyr Tyr Pro Asp Phe Asp Tyr Trp Gly Gln Gly Thr  
85 90 95

Leu Val Thr Val Ser Ser Ala Gly Gly Gly Ser Gly Gly Gly Gly Ser  
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln  
115 120 125

Pro Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Ser Cys  
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Ser Gly Asp Ala Leu Gly Asp Lys Tyr Ala Ser Trp Tyr Gln Gln Lys  
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Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Asp Asp Ser Asp Arg Pro  
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Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala  
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Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu Asp Glu Ala Asp Tyr Tyr  
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Cys Gln Ser Tyr Asp Gly Pro Asp Leu Trp Val Phe Gly Gly Gly Thr  
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Lys Leu Thr Val Leu Gly Gln Glu Phe Asp Tyr Lys Met Thr Met Thr  
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Lys Arg Ala Val Glu Pro Pro Ala Val  
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27

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cagtttagcc tgcaactgaa cagcgtgacc ccggaagata cggccgtgta ttattgcgcg 300  
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cagccgcctg ggaaagccct cgagtggctg gctctgattg attgggatga tgataagtat 180  
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gcgcagaagt ttcagggccg ggtgaccatt accgcggatg aaagcaccag caccgcgtat 240

atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtgttaat	300
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cctgggcagg gtctcgagt gatgggctgg attaaccga atagcggcg cacgaactac	180
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atggaactga gcagcctgcg tagcgaagat acggccgtgt attattgcgc gcgtggttat	300
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<212> DNA

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caggcgccag ttctggtgat ttatgatgat tctgaccgtc cctcaggcat cccggaacgc	180
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gacgaagcgg attattattg ccagagctat gactattctg ctgattatgt gtttggcggc	300
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<210> 68

<211> 324

<212> DNA

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caggcgccag ttctggtgat ttatgatgat tctgaccgtc cctcaggcat cccggaacgc	180
tttagcggat ccaacagcgg caacaccgcg accctgacca ttagcggcac tcaggcggaa	240

gacgaagcgg attattattg ccagagctat gactttgatt ttgctgtgtt tggcggcggc 300

acgaagttaa ccgttcttgg ccag 324

<210> 69

<211> 345

<212> DNA

<213> ARTIFICIAL SEQUENCE

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cctgaagact ttgcgactta ttattgccag cagactaata atgctcctgt tacctttggc	300
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85 90 95

Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg  
100 105 110

Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala  
115 120 125

Pro Ser Ser Gly Asp Asp Glu Asp Gly Glu Asp Glu Ala Glu Asp Thr  
130 135 140

Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp  
145 150 155 160

Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys  
165 170 175

Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly  
180 185 190

Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His  
195 200 205

Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly  
210 215 220

Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr  
225 230 235 240

Tyr Thr Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln  
245 250 255

Ala Gly Leu Pro Ala Asn Gln Thr Ala Val Leu Gly Ser Asp Val Glu  
260 265 270

Phe His Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu  
275 280 285

Lys His Val Glu Val Asn Gly Ser Lys Val Gly Pro Asp Gly Thr Pro  
290 295 300

Tyr Val Thr Val Leu Lys Val Ser Leu Glu Ser Asn Ala Ser Met Ser  
305 310 315 320

Ser Asn Thr Pro Leu Val Arg Ile Ala Arg Leu Ser Ser Gly Glu Gly  
325 330 335

Pro Thr Leu Ala Asn Val Ser Glu Leu Glu Leu Pro Ala Asp Pro Lys  
340 345 350

Trp Glu Leu Ser Arg Ala Arg Leu Thr Leu Gly Lys Pro Leu Gly Glu  
355 360 365

Gly Cys Phe Gly Gln Val Val Met Ala Glu Ala Ile Gly Ile Asp Lys  
370 375 380

Asp Arg Ala Ala Lys Pro Val Thr Val Ala Val Lys Met Leu Lys Asp  
385 390 395 400

Asp Ala Thr Asp Lys Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met  
405 410 415

Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala  
420 425 430

Cys Thr Gln Gly Gly Pro Leu Tyr Val Leu Val Glu Tyr Ala Ala Lys  
435 440 445

Gly Asn Leu Arg Glu Phe Leu Arg Ala Arg Arg Pro Pro Gly Leu Asp  
450 455 460

Tyr Ser Phe Asp Thr Cys Lys Pro Pro Glu Glu Gln Leu Thr Phe Lys  
465 470 475 480

Asp Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu  
485 490 495

Ala Ser Gln Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu  
500 505 510

Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg  
515 520 525

Asp Val His Asn Leu Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu  
530 535 540

Pro Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr  
545 550 555 560

His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe  
565 570 575

Thr Leu Gly Gly Ser Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe  
580 585 590

Lys Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ala Asn Cys Thr  
595 600 605

His Asp Leu Tyr Met Ile Met Arg Glu Cys Trp His Ala Ala Pro Ser  
610 615 620

Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Val Leu  
625 630 635 640

Thr Val Thr Ser Thr Asp Glu Tyr Leu Asp Leu Ser Ala Pro Phe Glu  
645 650 655

Gln Tyr Ser Pro Gly Gly Gln Asp Thr Pro Ser Ser Ser Ser Gly  
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